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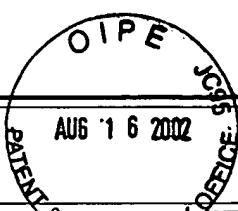
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- 1) General Transmittal Letter (in duplicate);
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Jane Massey Licata
Jane Massey Licata



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TRANSMITTAL LETTER
(General - Patent Pending)Docket No.
ISPH-0463

In Re Application Of: Monia et al.

Serial No.
09/575,554Filing Date
May 22, 2000Examiner
J. FredmanGroup Art Unit
1655

Title: ANTISENSE OLIGONUCLEOTIDE INHIBITION OF RAS

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Jane Massey Licata, Reg. No. 32,257

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Dated: August 16, 2002

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#15/Reply
Brief

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Attorney Docket No.: ISPH-0463

AUG 22 2002

Inventors: Monia et al.

Serial No.: 09/575,554

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Filing Date: May 22, 2000

Examiner: Jeffrey Norman Fredman

Group Art Unit: 1637

Title: Antisense Oligonucleotide Inhibition of RAS

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By Jane Massey
Typed Name: Jane Massey Licata, Reg. No. 32,257

U.S. Patent & Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

REPLY BRIEF

This is in reply to the Examiner's Answer mailed July 12, 2002.

I. Status of Claims

Appellants acknowledge that the obviousness-type double patenting rejection of the claims has been withdrawn in response to the terminal disclaimer filed on February 11, 2002.

II. Grouping of Claims

Appellants respectfully point out that the Appeal Brief as filed included a statement indicating that claims 1 and 7-20 would fall or stand together (see page 4 of the Brief as filed).

III. Response to the Examiner's Arguments

The Examiner suggests that Appellants have not identified any specific limitation which is missing in the rejection. Appellants respectfully point out that at pages 6-8, and in particular at page 8, of the Appeal Brief mailed on May 20, 2002 the specific limitation not taught by the cited prior art is clearly identified. This limitation is the recitation of specific sequences for antisense compounds to Ki-ras. As discussed in detail in Appellants' Brief, none of the references, including Bos et al., teach or suggest a specific sequence of an antisense compound targeted to Ki-ras as presently claimed. Therefore, Appellants respectfully submit that the cited combination of prior art fails to establish a *prima facie* case of obviousness as it fails to teach the claimed limitation, i.e., specific sequences of antisense

compounds targeted to Ki-ras. Therefore, this combination of art fails to meet the requirements for obviousness under 35 U.S.C. 103 (a) .

Appellants also respectfully disagree with the Examiner's suggestion that the cited art provides a reasonable expectation of success that the claimed specific antisense oligonucleotide sequences would successfully inhibit expression of Ki-ras. It is only with the specification in hand that one of skill has evidence of successful inhibition of Ki-ras using antisense oligonucleotides. Although there is similarity among the various ras genes, the art does not demonstrate inhibition of Ki-ras using antisense, and there is no teaching in any of the prior art cited of the antisense sequences as claimed.

Appellants also respectfully disagree with the Examiner's suggestion that the instant claims which recite "an oligonucleotide 8 to 30 nucleobases which comprises at least an 8-nucleobase portion" of an identified SEQ ID NO. is different than the language of the issued claim of U.S. Patent No. 6,117,848. The 6,117,848 patent claims "an oligonucleotide 8 to 30 nucleobases which comprises". The Examiner has cited another patent but Appellants' arguments are based on the 6,117,848 patent which was allowed by Examiner Fredman. As discussed in detail in the Appeal Brief, both claims use the open "comprising" language. Both claims are directed to portions of the cited sequences as small as 8

nucleobases. Appellants disagree with the Examiner's suggestion that the language of the 6,117,848 patent excludes (8 nucleobase portions) of the claimed sequences.

Appellants also respectfully point out that the unpredictability of the art of antisense is a consideration in this case. As discussed in the Appeal Brief, the data provided in the instant specification clearly showed that antisense oligonucleotides targeted to ras functioned in some cases to reduce expression while in the case of other antisense compounds targeted to the same regions, no such inhibition was seen (See Tables 2 and 11 of the specification as filed). This fact demonstrates to one of skill that since only certain antisense compounds targeted to ras had the ability to inhibit gene expression, success would not be expected based on the use of references showing activity to a target other than Ki-ras.

Respectfully submitted,

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Date: August 16, 2002

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